

IN THE CLAIMS:

Please cancel claims 1, 4-18, 20, 24, 26, 41 and 43 without prejudice or disclaimer.

2. (Thrice amended) A recombinant adenovirus with a significantly reduced tissue tropism for liver cells.

19. (Four times amended) A cell for producing a recombinant adenovirus having a tissue tropism for smooth muscle cells, said cell comprising:  
means for the assembly of said recombinant adenovirus wherein said means includes at least one adenovirus nucleic acid for the production of an adenoviral fiber protein, wherein said adenoviral fiber protein comprises at least a tissue tropism determining fragment of a subgroup B adenoviral fiber protein and wherein said cell is of PER.C6 (ECACC deposit number 96022940) origin.

37. (Four times amended) A method of reducing a tissue tropism of an adenovirus capsid for liver cells, said method comprising:

- i) exchanging a first nucleic acid encoding the tissue-tropism determining fragment of a fiber protein for a second nucleic acid encoding the tissue-tropism determining fragment of a fiber protein of adenovirus 16;
- ii) introducing the resulting nucleic acid from step i) into a cell capable of producing said adenovirus capsid; and
- iii) allowing said cell to produce said adenovirus capsid in a suitable medium.

38. (Amended) The recombinant adenovirus of claim 2 wherein said tissue tropism is provided by a virus capsid.

39. (Amended) The recombinant adenovirus of claim 38, wherein said virus capsid comprises protein fragments from at least two different viruses.

40. (Amended) The recombinant adenovirus of claim 39, wherein at least one of said viruses is an adenovirus.

42. (Twice Amended) The recombinant adenovirus of claim 40 wherein at least one of said protein fragments comprises a tissue tropism determining fragment of a fiber protein from a subgroup B adenovirus.

44. (Twice Amended) A recombinant adenovirus comprising increased tissue tropism for endothelial cells when compared to other recombinant adenovirus, wherein said tissue tropism is provided by a virus capsid and wherein said virus capsid comprises protein fragments from at least two different viruses.

45. (Amended) The recombinant adenovirus of claim 44 wherein at least one of said viruses is an adenovirus.

46. (Amended) The recombinant adenovirus of claim 45 wherein at least one of said viruses is a subgroup B adenovirus.

47. (Twice Amended) The recombinant adenovirus of claim 44 wherein at least one of said protein fragments comprises a tissue tropism determining fragment of a fiber protein of subgroup B adenovirus origin.

48. (Amended) The recombinant adenovirus of claim 46 wherein said subgroup B adenovirus is adenovirus 16.

49. (Twice Amended) The recombinant adenovirus of claim 44 wherein said protein fragments are of adenovirus subgroup C origin.

50. (Amended) The recombinant adenovirus of claim 44 wherein said virus capsid comprises protein fragments from at least two different viruses and wherein said protein fragments are from an adenovirus of subgroup C.

51. (Amended) The recombinant adenovirus of claim 44 further comprising an adenoviral nucleic acid.

52. (Twice Amended) The recombinant adenovirus of claim 51 wherein said adenoviral nucleic acid comprises sequences from at least two different adenoviruses.

53. (Amended) The recombinant adenovirus of claim 51 wherein said adenoviral nucleic acid comprises at least one sequence encoding a fiber protein comprising a tissue tropism determining fragment of a subgroup B adenovirus fiber protein.

54. (Amended) The recombinant adenovirus of claim 51 wherein said adenoviral nucleic acid is modified such that the capacity of said adenoviral nucleic acid to replicate in a target cell has been reduced or disabled.

55. (Amended) The recombinant adenovirus of claim 44, wherein said recombinant adenovirus comprises a minimal adenovirus vector or an Ad/AAV chimaeric vector.

56. (Amended) The recombinant adenovirus of claim 44 further comprising at least one non-adenoviral nucleic acid.

57. (Amended) The recombinant adenovirus of claim 56 wherein at least one of said non-adenoviral nucleic acids is a gene selected from the group of genes encoding a protein selected from the group consisting of: an apolipoprotein, a nitric oxide synthase, a herpes simplex virus thymidine kinase, an interleukin-3, an interleukin-1 $\alpha$ , an angiogenesis protein, an anti-angiogenesis protein, an anti-proliferation protein, a smooth muscle cell anti-migration protein, a vascular endothelial growth factor, a basic fibroblast growth factor, a hypoxia inducible factor 1 $\alpha$  and a PAI-1.

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Please add the following new claim:

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59

(New) The recombinant adenovirus of claim 47 wherein said subgroup B adenovirus is adenovirus 16.